

## **II. Remarks**

### **A. Status of the Specification**

The Specification has been revised to correct grammatical errors and address objections presented by the Action. No new matter has been added by these revisions.

### **B. Status of the Claims**

Claims 1-19 were pending when the Office Action was mailed from the U.S. Patent Office on January 14, 2005. Claims 1-3 have been canceled, claims 4, 6, and 19, have been amended, and claims 20-26 have been added. Support for these amendments and new claims can be found throughout the specification and claims as originally filed. See, for example, the specification at: page 7, paragraph 25; page 16, paragraph 73, line 3; page 23, Table 1 (*e.g.* compounds 5-9 and 11-13); and page 24, Table 2 (*e.g.*, compounds 5-9, 11-13 and 16 and 17). No new matter has been added. Claims 4-26 are therefore currently pending.

### **C. Objections to the Disclosure Are Overcome**

The Action objects to paragraph 13 of the specification by noting that there is no Ala-Asp bond in the amino acid sequence recited in the paragraph. The specification has been revised to address this objection. Therefore, Applicants request that this objection be withdrawn.

### **D. The Indefiniteness Rejections Are Overcome**

The Action rejects claims 1, 2, and 4-19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants disagree. The claims prior to any amendments made in this response were definite.

In an effort to further the prosecution, however, Applicants have amended the claims to address the concerns presented by the Action. This rejection is therefore moot and should be withdrawn.

**E. The Objections of Claims 1-19 Are Overcome**

The Action objects to claims 1-19 by noting that the term “val” should be “Val.” Claim 2 is separately objected to as being of improper dependent form. Applicants believe that these issues have been addressed in view the present claim amendments and requests that the objections be withdrawn:

**G. The Obviousness-Type Double Patenting Rejections Are Overcome**

The Action rejects claims 1-9 and 17-19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 102 and 112-115 of co-pending Application No. 10/343,654. Claims 10 to 16 have also been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 102 and 112-115 of co-pending Application No. 10/343,654 in view of WO 98/08871, Drucker, WO 99/43707 or Toft-Nielsen.

Applicants disagree. Claims 1-19 are not obvious in view of the cited references.

**1. The cited references do not disclose every element of claim 20**

Co-pending Application 10/343,654 discloses modified peptides comprising increased biological potency, prolonged activity and/or increased half-life. The modified peptides are obtained by the coupling of a conformationally rigid substituent at the N-terminal of the peptide. Non-limiting examples of rigidifying moieties coupled to the N-terminal of a GLP-1 peptide sequence are provided on page 41 of this co-pending Application (Example 1). WO 98/08871, Drucker, WO 99/43707, and Toft-Nielsen describe specific therapeutic roles for native GLP-1.

Even though a large number of possible rigidifying moieties for GLP-1 are suggested in co-pending Application 10/343,654, this reference is silent about the specific rigidifying moieties claimed in current claim 20. The other cited references also fail to disclose these specific rigidifying moieties. Claim 20 is therefore not obvious over the cited references. *See* MPEP § 2142 (noting that “[t]o establish a *prima facie* case of obviousness ... the prior art reference (or references when combined) must teach or suggest all the claim limitations.”); *see also In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

**2. There is no reasonable expectation of success that the combination of references or modifications to the references would work**

A second requirement necessary to establish a *prima facie* case of obviousness requires a showing by the Examiner of “a reasonable expectation of success” that the combination of references or modifications would work. *See id.* This has not been done.

Co-pending Application 10/343,654 does not disclose the rigidifying moieties of present claim 20. This reference also does not disclose or suggest Applicants’ observed biological activity of the GLP-1 analogues or any structure-activity relationship. Further, the Action provides no factual evidence that Applicants’ claimed rigidifying moiety would have been predicted to have had an increase biological potency when compared to that of native GLP-1.

Applicants specification, by contrast, provides data showing that the slightest change in the structure of the rigidifying moiety can have an impact on the activity of a GLP-1 analogue. *See, e.g.*, Figure 1; *see also* Examples 3, 5, and 6. These data show that certain changes in the rigidifying moiety can produce a compound that is superior to native GLP-1. This is evidence of non-obviousness. *See* MPEP § 2143.02 (noting that “at least some degree of predictability is required” to establish a reasonable expectation of success”). Therefore, there is no reasonable expectation of success that modifying or combining the cited references would work.

For at least the reasons discussed above, the present claims are not obvious over the cited references. Applicants request that this obviousness-type double patenting rejection be withdrawn.

#### **H. The Anticipation and Obviousness Rejections Are Overcome**

The Examiner rejects claims 1, 4-6, 17, and 19 under 35 U.S.C. § 102(b) and claims 2 and 3 under 35 U.S.C. § 102(a) and (e) as being anticipated by WO 02/10195. The Examiner also alleges that claims 7-16 and 18 are obvious under 35 U.S.C. § 103(a) in view of this application.

Applicants disagree. The present claims are not anticipated or rendered obvious over the cited reference.

WO 02/10195 is the PCT application from which derives co-pending Application 10/343,654. Because of this, the arguments presented in the above sections are relevant to this rejection. These arguments are incorporated by reference.

Based on the above arguments, it is apparent that the present claims are not anticipated nor rendered obvious over the WO 02/10195 application. Applicants request that these rejections be withdrawn.

#### **I. Conclusion**

Applicants believe that the present document is a full and complete response to the Office Action dated January 14, 2005. Applicants submit that the present case is in condition for allowance and such favorable action is requested.

### **III. Petition for a One-Month Extension of Time:**

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for an extension of time of one months to and including May 15, 2005, in which to respond to the Office Action dated January 14, 2005. Pursuant to 37 C.F.R. § 1.17, a check in the amount of \$60.00 is enclosed, which is the process fee for a one-month extension of time for a small entity status. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski Deposit Account No. 50-1212/GOUD:038US.

Should the Examiner have any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-3020.

Respectfully submitted,



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